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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/825,068	04/14/2004	Chih-Ping Liu	55600-8014.US03	7994

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EXAMINER	
HISSONG, BRUCE D	
ART UNIT	**PAPER NUMBER**
1646	

MAIL DATE	DELIVERY MODE
06/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/825,068	LIU ET AL.	
	Examiner	Art Unit	
	Bruce D. Hissong, Ph.D.	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 April 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6,8,10 and 11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6,8,10 and 11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *3/6/07, 4/17/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4/17/2007 has been entered.

2. Claims 1, 3-4, 6, 8, and 10-11 are currently pending and are the subject of this office action.

Information Disclosure Statement

1. The information disclosure statement received on 3/6/2007 has been fully considered by the Examiner.

2. The information disclosure statement received on 4/17/2007 has been fully considered by the Examiner. Citations 2, 3, and 4 of have been lined-through because they were cited in the information disclosure statement received on 3/6/2007.

Claim Rejections - 35 USC § 112, first paragraph - enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 3-4, 6, 8, and 10-11 *remain rejected* under 35 USC § 112, first paragraph, regarding lack of enablement for a method of increasing the IL-10/IL12 blood ratio in a subject suffering from multiple sclerosis, wherein said method comprises oral administration of any IFN-τ polypeptide other than those of SEQ ID NOs 2 or 3, as set forth on pages 4-5 of the office

action mailed on 4/24/2006, pages 3-4 of the office action mailed on 10/17/2006, and the advisory action mailed on 3/13/2007.

The claims of the instant invention recite a method of increasing the IL-10/IL-12 blood ratio in a subject suffering from multiple sclerosis, wherein said method comprises orally administering an IFN-τ polypeptide having a sequence that is 80% identical to the polypeptide of SEQ ID NO: 2.

In the response received on 1/17/2007, the Applicants argue that the specification is enabling for methods of increasing the IL-10/IL-12 blood ratio in a subject suffering from multiple sclerosis by oral administration a of polypeptide having less than 100% identity to SEQ ID NO: 2 because IFN-τ is well-known in the art and has been extensively studied for 20 years, including studies on structure/function relationships, and numerous IFN-τ sequences are well-known in the art, such as those disclosed in paragraph 0036 of the specification. Furthermore, the Applicants argue that the disclosure of the specification combined with that of the prior art would allow a person of ordinary skill in the art to easily test a polypeptide for IFN-τ activity, and to determine whether or not it is capable of increasing the blood IL-10/IL-12 ratio in a subject suffering from multiple sclerosis.

These arguments have been fully considered and are not persuasive. As written, the claims read on administration of any polypeptide with 80% identity to the polypeptide of SEQ ID NO: 2. Because the claims encompass administration of polypeptides with the ability to increase the IL-10/IL-12 blood ratio, but also any other type of polypeptide related to IFN-τ only by percent identity, the breadth of the claims is excessive. Although the specification and the prior art identify numerous sequences for IFN-τ, and IFN-τ is well-known in the art, the claims read on administration of many potential non-IFN-τ polypeptides. One of ordinary skill in the art would not be able to predict which of the many possible polypeptides having 80% identity to SEQ ID NO: 2 would possess the ability to increase the IL-10/IL-12 blood ratio in subjects suffering from multiple sclerosis. Thus, although a skilled artisan would be able to make a polypeptide having 80% identity to SEQ ID NO: 2 and test it for the ability to increase the IL-10/IL-12 blood ratio, the standard for enablement is to be able to make and *use*, rather make and *test* an invention. A skilled artisan would therefore not be able to make and then use all other possible polypeptides having 80% identity to SEQ ID NO: 2 without further, undue experimentation.

Furthermore, although IFN-τ structure/function relationships have been studied previously, a skilled artisan would still be unable to predict the effect of mutating or altering all residues of the SEQ ID NO: 2 primary amino acid sequence in order to create a polypeptide having 80% identity to SEQ ID NO: 2. It is known in the art that even single amino acid changes or differences in the amino acid sequence of a protein can have dramatic effects on the protein's function. As an example highlighting the unpredictable effects of mutations on protein function, Mickle *et al* (Med. Clin. North Am., 2000, Vol. 84(3), p. 597-607) teaches that cystic fibrosis is an autosomal recessive disorder caused by abnormal function of a chloride channel, referred to as the cystic fibrosis transmembrane conductance regulator (CFTR – p. 597). Several mutations can cause cystic fibrosis, including the G551D mutation. In this mutation, a glycine replaces the aspartic acid at position 551, giving rise to the cystic fibrosis phenotype. In the most common cystic fibrosis mutation, Δ-F508, a single phenylalanine is deleted at position 508, giving rise to the cystic fibrosis phenotype. Thus, even the substitution or deletion of a single amino acid can have dramatic and *unpredictable* effects on the function of the protein. The specification does not disclose which amino acids or regions of SEQ ID NO: 2 are critical for maintenance of protein function, or which amino acids or regions can be altered. Therefore, a person of ordinary skill in the art would therefore require further, undue experimentation in order to make and use an IFN-τ polypeptide having less than 100% identity to SEQ ID NO: 2 in a manner commensurate in scope with the claims.

In summary, the breadth of the claims is excessive because the claims read on oral administration of any polypeptide that is 80% identical to SEQ ID NO: 2, regardless of whether or not the polypeptide is an IFN-τ polypeptide or is capable of increasing the IL-10/IL-12 blood ratio. Because one of ordinary skill in the art would not be able to predict the effects of non-IFN-τ polypeptides that are 80% identical to SEQ ID NO: 2, and the lack of guidance and examples in the specification showing how to use such polypeptides in the claimed method, a person of ordinary skill in the art would require further, undue experimentation to practice the instant invention commensurate with the full scope of the claims. However, if Applicants provide a listing and alignment of IFN-τ sequences, pointing out which amino acids/regions are conserved and are necessary for function (i.e. the ability to increase the IL-10/IL-12 blood ratio), this rejection may be reconsidered.

Claim Rejections - 35 USC § 112, first paragraph – written description

Claims 1, 3-4, 6, 8, and 10-11 *remain rejected* under 35 USC § 112, first paragraph, regarding lack of written description for the genus of polypeptides having less than 100% identity to the IFN-t sequence of SEQ ID NO: 2, as set forth on pages 6-7 of the office action mailed on 4/24/2006, page 5 of the office action mailed on 10/17/2006, and the advisory action mailed on 3/13/2007.

In the response received on 1/17/2007, the Applicants argue that the specification adequately describe the claimed genus of polypeptides having less than 100% identity to SEQ ID NO: 2 because the specification teaches IFN-τ sequences which are well-known in the art (paragraph 0036). Furthermore, the Applicants assert that a person of ordinary skill in the art would not need to make predictions as to how to alter the sequence of an IFN-τ polypeptide because the prior art discloses structure/function relationships of IFN-τ polypeptides and thus shows where changes can be made.

These arguments have been fully considered and are not persuasive. As stated *supra*, the claims are drawn to administration of any polypeptide sequence that is 80% identical to SEQ ID NO: 2. Given the broadest reasonable interpretation, the claims are thus drawn to a genus of polypeptides defined only by sequence identity to SEQ ID NO: 2, and which may or may not possess the ability to increase the IL-10/IL-12 blood ratio in a subject suffering from multiple sclerosis. Although a person of ordinary skill in the art could envision the genus of IFN-τ polypeptides as disclosed in the art, a skilled artisan could not conceive every possible polypeptide having 80% identity to SEQ ID NO: 2 and the ability to increase the IL-10/IL-12 blood ratio in a subject. Furthermore, based on the teachings of Mickle *et al*, as described *supra*, one of ordinary skill in the art would not necessarily be able to predict which regions or amino acids could be mutated in order to create a polypeptide that is 80% identical to the polypeptide of SEQ ID NO: 2 and still retain the desired biological activity. The specification teaches that conservative substitutions can be made in IFN-τ polypeptides, but does not disclose which specific regions or residues can be altered, and which regions are critical for the desired function.

Therefore, it is not clear from the instant specification that Applicants did indeed possess the genus of polypeptides encompassed by the claims as currently written, and therefore, owing to the large size of this genus and the lack of teachings in the specification to adequately describe this genus in terms of regions or residues that can be modified and still result in a

polypeptide capable of increasing the IL-10/IL-12 blood ratio in a subject, the instant specification lacks adequate written description for all polypeptides having only 80% identity to SEQ ID NO: 2. However, if Applicants provide a listing and alignment of IFN-τ sequences, pointing out which amino acids/regions are conserved and are necessary for function (i.e. the ability to increase the IL-10/IL-12 blood ratio), this rejection may be reconsidered.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3-4, 6, 8, and 10-11 *remain rejected* under 35 USC § 103(a) as being obvious in view of the combination of Soos *et al* ("Soos"), van Boxel-Dezaire *et al* ("van Boxel-Dezaire") and Petereit *et al* ("Petereit"), as set forth on pages 7-8 of the office action mailed on 4/24/2006, pages 5-7 of the office action mailed on 10/17/2006, and the advisory action mailed on 3/13/2007.

In the response received on 1/17/2007, the Applicants argue that the claims of the instant invention are not obvious in view of the combination of Soos, van Boxel-Dezaire, and Petereit because neither Soos, van Boxel-Dezaire, nor Petereit teach the claimed IFN-τ dosage, nor do they suggest the claimed IFN-τ dosage. The Applicants also assert that there is nothing in the teachings of Soos alone, or in combination with van Boxel-Dezaire and Petereit, that suggests increasing the dosage of IFN-τ beyond what is disclosed in Soos. For these reasons, the Applicants argue that a prima facie case for obviousness has not been made because the limitations of the claims are not taught or suggested by Soos, van Boxel-Dezaire, and Petereit. These arguments have been fully considered and are not persuasive. As set forth in the previous office actions, the combinantion of Soos, Boxel-Dezaire, and Petereit teach administration of IFN-τ for treatment of multiple sclerosis, decreased IL-10 levels in multiple sclerosis patients, and a correlation of decreased IL-10 and higher disability scores. Also taught is that administration of IFN-τ increases IL-10 levels. Thus, the combined disclosures of these references provide the motivation to administer IFN-τ to increase the IL-10/IL-12 blood ratio in

multiple sclerosis pateints. Because the combined references do not teach away from the claimed dosage, the results of the instant application would not be unexpected. Furthermore, one of ordinary skill in the art would always have the motivation, and the ability, to optimize the dosage of a therapeutic regime that has already been disclosed in the art as effective for a particular disease. MPEP 2144.05 states:

"[W]here the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation." *In re Aller*, 220 F.2d 454, 454, 105 USPQ 223, 235, (CCPA 1955).

Therefore, because the combination of Soos, van Boxel-Dezaire, and Petereit provide the motivation and a reasonable expectation of success in practicing a method of administering IFN-τ to increase the IL-10/IL-12 blood ratio in a subject suffering from multiple sclerosis, and the ability and motivation of a skilled artisan to optimize the IFN-τ dosage by routine optimization, the claims of the instant invention are obvious in view of Soos, van Boxel-Dezaire, and Petereit.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

1. Rejection of claims 1, 3-4, 6, 8, and 10-11 on the grounds of nonstatutory obviousness-type double patenting as being unpatentable over co-pending applications 10/825,382, 10/825,457, 10/824,710, 11/040,706, and 10/884,741, as set forth on pages 9-10 of the office action mailed on 4/24/2006 and pages 7-8 of the office action mailed on 10/17/2006, is *withdrawn* in response to Applicants' submission of a terminal disclaimer for these applications.

2. Claims 1, 3, 4, 6, 8, 10, and 11 remain provisionally rejected under the judicially-created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 17, and 18 of co-pending application 11/112,369, is maintained for reasons of record set forth in the previous office actions. In the response received on 1/17/2007, the Applicants argue that not all multiple sclerosis patients exhibit decreased IL-10 levels, and therefore identifying a multiple sclerosis patient would not inherently identify a patient having an IL-10 deficiency. This argument has been fully considered and is not persuasive. As stated in the previous office actions, it is known in the art that multiple sclerosis patients have decreased IL-10 levels. Even if not all multiple sclerosis patients exhibit IL-10 deficiency, the method of the instant application seeks to administer IFN-τ for the purpose of increasing IL-10 levels. Thus, a skilled artisan would find it obvious to identify patients with IL-10 deficiency in the practicing of the instant application. It is also noted that the method steps of administering IFN-τ in the instant application is identical to those of the '369 application.

Conclusion

No claim is allowable.

All claims are drawn to the same invention claimed in the parent application prior to the filing of this Continued Prosecution Application under 37 CFR 1.53(d) and could have been finally rejected on the grounds and art of record in the next Office action. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing under 37 CFR 1.53(d). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no, however, event will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Bruce D. Hissong, Ph.D., whose telephone number is (571) 272-3324. The examiner can normally be reached M-F from 8:30 am - 5:00 pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, Ph.D., can be reached at (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

BDH
Art Unit 1646

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